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A feasibility study of trans-subclavian TAVI with the Lotus valve

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Short title: Subclavian TAVI using the Lotus valve

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Abstract

Objectives

To assess the feasibility of subclavian transcatheter aortic valve implantation (TAVI) using the Lotus valve.

Background

TAVI is used to treat patients with severe aortic stenosis, with trans-femoral (TF) access being the safest and most widely used route. In the significant minority of patients unsuitable for this, there are reports that the subclavian artery may be safest alternative access route. The Lotus device is a fully retrievable 2nd generation transcatheter heart valve which is licensed for femoral and trans-aortic access. There are limited data on the suitability of this valve for subclavian access.

Methods

We assessed the feasibility of trans-subclavian TAVI with the Lotus valve in patients unsuitable for TF TAVI. Between January and October 2016, we identified 10 patients who underwent trans-subclavian TAVI with the Lotus valve. This cohort was compared with 347 (85%) patients who underwent trans-femoral TAVI, 45 (11%) patients who underwent and trans-apical or direct-aortic TAVI and the total group of 16 (4%) patients who underwent subclavian TAVI.

Results

10 patients aged 75 years (69-83) underwent attempted TAVI with the Lotus via subclavian access. Procedural success was 100%. In-hospital and 30-day mortality was zero. There were no nerological eventss, no vascular complications and no myocardial infarctions. 4 of 10 patients required a pacemaker post TAVI. No patient was left with moderate or greater aortic regurgitation. Median length of stay was 3 days post-procedure.

Conclusions

TAVI with the Lotus valve is feasible via the subclavian artery and appears safe with excellent outcomes in our patients..

Introduction

Aortic stenosis is the most common form of valvular heart disease in Europe and North America [1,2]. Transcatheter aortic valve implantation (TAVI) reduces mortality compared with medical therapy in patients deemed to be high risk with surgical aortic valve replacement (SAVR)[3]. In patients with high or intermediate surgical risk, TAVI achieves similar survival at 1 year to SAVR[4,5] and is recommended by both American and European guidelines in patients with high surgical risk[6,7].

TAVI is most commonly performed via the femoral artery [8,9]. Trans-femoral access is associated with lower rates of mortality when compared to other routes[10,11] which has led most operators to adopt a "trans-femoral first" access strategy. TAVI requires relatively large sheaths (minimum 14-Fr) and delivery catheters and the transfemoral approach may not be feasible in patients with unsuitable vasculature. The trans-aortic and trans-apical are the most commonly used alternative access routes but have disadvantages including the greater invasiveness of a surgical thoracotomy[12]. The trans-subclavian approach to TAVI was initially described using the CoreValve (Medtronic, USA)[13] and subsequently using the Sapien valve (Edwards, USA)[14]. Evidence is emerging that the trans-subclavian route is safe[15]. Observational data have demonstrated that survival following subclavian access is not significantly different from survival following TF access while survival following trans-aortic/trans-apical access was significantly lower than trans-femoral and subclavian access[16,17].

The Lotus System (Boston Scientific, USA) is a 2nd generation trans catheter heart valve approved for use in Europe in October 2013 and currently under evaluation in the USA. It is fully repositionable and retrievable, designed to facilitate precise delivery[18] and has excellent results at 1 year, particularly in minimising para-valvular aortic regurgitation[19]. This is particularly important as moderate or greater para-valvular regurgitation is associated with increased mortality following TAVI[5,20]. Initially implanted via the femoral route, the valve is now licensed for trans-aortic access also. The Lotus valve is currently not licensed in Europe for trans-subclavian access although there is is one report of the Lotus valve being delivered successfully via the subclavian artery[21].

Methods

Between December 2008 and October 2016, our institution (Queen Elizabeth Hospital Birmingham, UK) performed 408 TAVI procedures. Demographic, procedural and outcome data were entered prospectively to the National Institute for Cardiovascular Outcomes Research database. The preferred access site was the femoral artery and this was used in 347 (85%) patients. Forty-six (11%) patients underwent trans-aortic/tran-apical access and 16 (4%) underwent trans-subclavian access of whom 10 underwent attempted TAVI with the Lotus Valve (Boston Scientific, USA). Valve types implanted were Edwards Sapien (Irvine, CA, USA), 24 (5.8%); Edwards Sapien XT, 131 (32.1%); Edwards Sapien 3, 213 (52.2%), Lotus valve, 33 (8%); CoreValve (Medtronic, USA) 3 (0.7%); Evolute R (Medtronic, USA) 3 (0.7%). Between January and October 2016, 10 patients who were unsuitable for transfemoral TAVI underwent the procedure using the Lotus valve via the left subclavian artery.

All patients underwent a gated cardiac muti detector CT (MDCT)and helical MDCT of the aorta and ilio-femoral vessels. All patients were assessed by the Heart Team as being unsuitable for open heart surgery.

Lotus Valve

The Lotus valve consists a woven, nitinol wire, self-expanding frame to which is mounted a bovine pericardial aortic valve and is designed for catheter based introduction. The valve is expanded via controlled mechanical expansion. Rapid pacing is not required during valve deployment; the valve functions early in the deployment cycle and can be repositioned or fully retrieved at any point before uncoupling and valve release. An outer adaptive seal is designed to minimize paravalular leak. Currently 3 valve sizes are available; 23, 25 and 27 mm and are suitable for an aortic valve annulus in the range ≥19mm and ≤27mm. The 23mm valve is introduced through an 18F sheath and the 25 and 27mm devices through a 20F sheath. The 18F sheath requires a vessel lumen of ≥6mm and the 20F requires a vessel lumen of ≥6.5mm.

Patient selection

10 patients unsuitable for trans-femoral access with any device used at our institution were selected for Lotus implantation if their left subclavian artery was of suitable calibre for Lotus sheath introduction, if there was absence of concentric calcification and if annular area assessed by CT was within the recommended range for the Lotus device (currently ≥314mm^2 to ≤572mm^2). Assessment was made from the screening MDCT undertaken in all patients to assess access route.

Subclavian access

All procedures were performed under general anaesthesia with TOE monitoring. The left subclavian artery was exposed surgically and a suitable access area was identified by inspection and palpation. Using a Seldinger technique the subclavian artery was punctured within a purse string suture and a 5F 11cm sheath was introduced. Over a soft J-tipped 0.035" wire a 5F Judkins right catheter was positioned in the ascending aorta and the soft 0.035" wire exchanged for a 180cm Super Stiff 0.035" Amplatz wire. Over the stiff wire the 20F Lotus sheath was introduced with the distal tip placed in the ascending aorta under fluoroscopic guidance. The aortic valve was crossed and a 0.035" small or extra small Safari Wire (Boston Scientific, USA) was placed in the left ventricle. Pre-dilatation was not performed in any patient. The Lotus valve was then introduced through the Lotus sheath with the catheter in an 'S' configuration and implanted with standard technique.

Statistical methods

The populations were described using median and interquartile range for continuous variables and percentage for categorical variables. Statistical analysis was performed using STATA (College Station, USA).

The study complies with the Declaration of Helsinki. The data were collected as part of a mandatory UK national cardiac audit and all patient identifiable fields were removed before analysis. The study complies with section 251 of the National Health Service Act 2006. Ethical approval was not required under research governance arrangements for analyses.

Results

Baseline Demographics

Baseline demographics are shown in table I.

Patients who received transaortic/transapical TAVI had significantly higher Logistic Euroscore than the patients undergoing transfemoral TAVI (19 vs 14; p0.001). Logistic Euroscore was also numerically higher in the entire subclavian cohort compared with the transfemoral group, although this did not meet significance (22 vs 14; p=0.07). The transaortic/transapical and entire subclavian group more frequently had peripheral vascular disease than the transfemoral cohort (p<0.001).

The 10 patients who underwent trans-subclavian TAVI were aged 75 years (69-83) with 60% being male. Compared with the trans-femoral group the cohort undergoing trans-subclavian TAVI with Lotus had more frequently undergone open heart surgery, had a greater frequency of peripheral vascular disease, diabetes and a higher BMI. Characteristics of the Lotus subclavian group were similar to the cohort who received trans-aortic or trans-apical TAVI.

Procedural characteristics

The majority of femoral TAVI cases were carried out under local anaesthetic whilst all trans-subclavian cases and all transaortic/transapical cases were performed under general anaesthetic. The rates of post -dilatation and choice of TAVI valve used can also be seen in table II.

Outcomes

Procedural outcomes are shown in table III.

Procedural success, defined as a successful attempt to implant a valve to the annulus, was high in the whole cohort with the valve implanted successfully in 99% of patients. In the entire population rates of major complications including in-hospital death (4.7%), 30-day mortality (4.4%), peri-procedural MI (1.6%), peri-procedural stroke (0.8%) and major access site complications (2.3%) were low. The requirement for permanent pacing post TAVI and before discharge was 7.4%.

All 10 patients undergoing trans-subclavian with Lotus required a 20F sheath for a 25 or 27mm valve. The sheath was successfully passed into the ascending aorta in 9 patients. In one patient, the tip of the sheath would not pass an area of calcification in the proximal subclavian artery, however, the delivery sheath, being of narrower diameter, successfully traversed the obstruction and the valve was deployed uneventfully. There was no haemodynamic instability or ECG evidence of ischaemia in any of the 4 patients with patent IMAs during the procedure following introduction of the sheath. Procedural success was achieved in all patients. Passage of the Lotus THV to the native aortic valve was uncomplicated in all patients. Due to the short distance from the access site to the native aortic valve and as the catheter was delivered in an 'S' configuration, the catheter naturally self-oriented and proved extremely easy to deliver. Post implant valve gradients were low and no patient required valvuloplasty post valve deployment. 4 of the 10 patients (40%) required a pacemaker due to heart block at the end of the procedure. None of these patients had pre-existing conduction abnormalities such as right bundle branch block or first degree heart block on electrocardiogram. There were no vascular complications or access site related problems in any of the 10 patients. 2 patients with morbid obesity (BMI 40 and 47) were extubated on ITU. The remaining 8 patients were extubated

immediately after TAVI in the catheter laboratory and then transferred directly to the coronary care unit. Patients were able to mobilise quickly after the procedure. The median length of stay was significantly lower in the entire subclavian group compared with the transapical/transaortic group (3 days vs 7 days, p<0.001). Significantly more patients in the transaortic/transapical group (28%) required blood transfusions than the transfemoral group (9%) or subclavian group (6%). No statistical difference was seen in the rate of blood transfusion between the subclavian and transfemoral groups. The transaortic/transapical group more frequently required dialysis than either the subclavian or transfemoral groups.

Peak CRP and peak total CPK were both significantly higher in the transapical/transaortic cohort compared with the entire subclavian group. 67% of patients in the transapical/transaortic group required a chest drain compared with 0% in the subclavian group.

Discussion

Our study demonstrates that TAVI via the subclavian artery using the Lotus valve is feasible and safe with similar outcomes to those receiving transfemoral TAVI. The valve was deployed successfully in all 10 patients with no major complications (death, peri-procedural stroke or MI, access site problems) until discharge. This is the largest reported series of patients to have undergone TAVI via the subclavian artery with the Lotus valve. It should be noted that in this cohort of patients there was a relatively high requirement for permanent pacing either during or immediately following the procedure (40% of patients). A high rate of requirement for permanent pacing of 28.6% was also originally described with use of the valve from the femoral artery[22]. None of the patients in our cohort of patients had moderate or severe paravalvular regurgitation.

Patients who underwent subclavian TAVI had fewer deaths and TIA/stroke than the cohort of patients who underwent transapical or direct aortic TAVI. Although both groups of patients required general anaesthesia and surgical cut down, transapical and direct aortic access are more invasive due to the need for a sternotomy or thoracotomy, and the requirement to open the pericardium. Transaortic/transapical access was associated with a higher need for blood transfusion than subclavian access and these patients also usually required a chest drain immediately following the procedure. The greater invasiveness of transaortic/transapical access was reflected in the markedly higher peak CRP compared with the subclavian cohort. CRP is a marker of the systemic inflammatory response[23] and a high CRP post cardiothoracic surgery is associated with a higher risk of major cardiovascular adverse events[24].

Further evidence of the more invasive nature of transapical/transaortic access was the observation that these patients experienced longer lengths of stay both in the intensive care unit and in hospital compared to patients who underwent subclavian TAVI. This has important beneficial implications of subclavian access for both for patients, who enjoy a reduced hospital stay, and healthcare providers by reducing overall costs.

Study limitations

The main limitation of our study is that the cohort of patients who underwent subclavian TAVI via the subclavian artery was relatively small at 16 patients. A further limitation is that this is not a randomised study. Finally, we do not yet have long term follow up data on the group of patients who had subclavian TAVI using Lotus.

Conclusion

In our cohort of patients, TAVI with the lotus valve using a trans-subclavian approach was safe and had outcomes comparable to TAVI via the transfemoral route. Patients who underwent trans-subclavian TAVI had significantly fewer complications and required a shorter hospital stay than those undergoing transaortic or direct apical procedures. Our data are consistent with the growing body of evidence that suggests subclavian access is safer and less invasive than transaortic/transapical access and may be the preferred alternative access.

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Table I - Baseline demographics of patients undergoing TAVI

Variable	Subclavian (all) (n= 16)	Subclavian (Lotus)(n=10)	Transapical and direct aortic (n=45)	Femoral (n= 347)	P value femoral vs transaortic/ transapical*	P value femoral vs subclavian*	P value subclavian vs transaortic/ transapical*
Age, years	78 [72-84]	75 [69-83]	81 [75-85]	83 [78-86]	0.38	0.20	0.83
Male sex	12 (75%)	6 (60%)	24 (53%)	190 (55%)	0.86	0.11	0.13
Logistic Euroscore	19 [15-24]	22 [17-28]	21 [15-31]	14 [10-24]	0.001	0.07	0.77
BMI	29.0 [26.4-34.6]	30.9 [26.8-36.2]	26.7 [23.5-29.4]	26.7 [24.1-30.6]	1.00	0.44	0.71
Diabetes	6 (38%)	5 (50%)	12 (27%)	107 (31%)	0.57	0.57	0.41
Creatinine	88 [80-115]	81 [80-89]	92 [77-131]	93 [77-125]	0.92	0.54	0.43
Previous MI	7 (44%)	5 (50%)	15 (33%)	77 (22%)	0.10	0.05	0.46
Previous PCI	6 (38%)	5 (50%)	8 (18%)	76 (22%)	0.53	0.15	0.11
Previous cardiac surgery	1 (6%)	1 (10%)	3 (7%)	23 (7%)	0.75	0.29	0.47
Previous pacemaker	5 (31%)	4 (40%)	10 (22%)	70 (20%)	0.99	0.95	0.95
Current or Ex-Smoker	15 (94%)	9 (90%)	34 (76%)	194 (56%)	0.01	0.003	0.12
Atrial fibrillation	6 (38%)	3 (30%)	14 (31%)	87 (25%)	0.38	0.27	0.64
Pulmonary hypertension (>60mmHg)	0 (0%)	0 (0%)	31 (69%)	115 (33%)	<0.001	0.005	<0.001
Chronic lung disease	9 (56%)	5 (50%)	14 (31%)	82 (24%)	0.27	0.003	0.08
TIA/CVA	5 (31%)	4 (40%)	6 (13%)	63 (18%)	0.42	0.19	0.11
Peripheral vascular disease	13 (81%)	9 (90%)	25 (56%)	73 (21%)	<0.001	<0.001	0.07
AV peak gradient	74 [65-78]	74 [60-77]	78 [65-96]	71 [60-85]	0.11	0.59	0.22

(mmHg)							
AV area (cm^2)	0.7 [0.6-0.8]	0.8 [0.6-0.8]	0.6 [0.5-0.7]	0.6 [0.5-0.8]	0.008	0.79	0.10
Aortic annulus (mm)	25 [24-27]	24 [24-25]	23 [21-25]	24 [22-25]	0.26	0.09	0.16
LV >50% **LV 30-49%** **LV <30%**	12 (75%) 2 (13%) 2 (13%)	7 (70%) 1 (10%) 2 (20%)	10 (22%) 30 (67%) 5 (11%)	202 (58%) 102 (29%) 43 (12%)	<0.001	0.32	<0.001

*P-values based on Person chi^2 comparing medians for continuous variables and chi^2test for categorical variables.

Table II – Procedural characteristics

	Subclavian (all) (n= 16)	Subclavian (Lotus)(n=10)	Transapical and direct aortic (n=45)	Femoral (n= 347)	P value femoral vs transaortic/ transapical*	P value femoral vs subclavian*	P value subclavian vs transaortic/ transapical*
Local anaesthesia	0 (0%)	0 (0%)	0 (0%)	210 (61%)			
Post dilatation of the implanted valve	3 (19%)	0 (0%)	2 (13%)	81 (29%)	0.16	0.40	0.63
Lotus	10	10	1	22			
Sapien/S3/XT	2	0	44	323			
Evolute R/Corevalve	4	0	0	2			

Table III - Outcomes in patients undergoing TAVI

	Subclavian (all) (n= 16)	Subclavian (Lotus)(n= 10)	Transapical and direct aortic (n= 45)	Femoral (n= 347)	P value femoral vs transaortic/ transapical*	P value femoral vs subclavian*	P value subclavian vs transaortic/ transapical*
Procedural success	16 (100%)	10 (100%)	44 (98%)	343 (99%)	0.55	0.67	0.55
In hospital death	0 (0%)	0 (0%)	5 (11%)	14 (4%)	0.04	0.41	0.16
30 day mortality	0 (0%)	0 (0%)	5 (11%)	13 (4%)	0.03	0.43	0.16
Stroke/TIA to discharge	0 (0%)	0 (0%)	2 (4%)	1 (0.3%)	0.003	0.83	0.39
Tamponade	0 (0%)	0 (0%)	1 (2%)	10 (3%)	0.80	0.49	0.55
Periprocedural MI	0 (0%)	0 (0%)	1 (2%)	5 (1%)	0.69	0.63	0.55
AR by echo (moderate or more)	0 (0%)	0 (0%)	0 (0%)	4 (1%)	0.47	0.67	-
Emergency valve in valve	1 (6%)	0 (0%)	0 (0%)	2 (0.6%)	0.61	0.01	0.09
Major access site complication	0 (0%)	0 (0%)	2 (4%)	13 (4%)	0.82	0.43	0.39
Permanent pacemaker during or post procedure	6 (38%)	4 (40%)	2 (4%)	22 (6%)	0.62	<0.001	0.001
New haemofiltration or dialysis	0 (0%)	0 (0%)	5 (11%)	15 (4%)	0.05	0.40	0.16
Blood transfusion	1 (6%)	0 (0%)	11 (28%)	28 (9%)	<0.001	0.73	<0.001
LOS (length of stay)	3 [2-3]	3 [2-3]	7 [5-11]	3 [2-5]	<0.001	0.19	<0.001
LOS (in ICU)	0 [0-0]	0 [0-1]	2 [1-4]	-	-	-	0.001

Peak CRP	57 [43-89]	53 [28-74]	197 [138-278]	-	-	-	<0.001
Peak CK	167 [93-202]	150 [104-244]	270 [197-444]	-	-	-	0.003
Chest drain	0 (0%)	0 (0%)	30 (67%)	-	-	-	<0.001

*P-values based on Person chi^2 comparing medians for continuous variables and chi^2 test for categorical variables.